

REMARKS AND RESPONSE

A. Status of the Claims

Claims, 5-10 have been canceled, claims 25 and 35 have been amended and new claim 43 has been added. Thus, claims 25-43 are currently pending in the case. Support for the amendment to claim 25 can be found, at least, on page 45 lines 11-19 of the specification. Support for new claim 43 can be found in previous claim 25.

B. Rejections Under 35 U.S.C. § 103

Rejection of Claims 5-6, 9, 25-30 and 39-42 as obvious over Coffee in view of McDonald or Yang

The Examiner has asserted a new rejection of the instant claims over Coffee in view of McDonald or Yang. However, the Examiner has failed to make a *prima facie* case for obviousness under 35 U.S.C. §103. Applicants have canceled claims 5-10 and claims 25-44 concern methods for using cationic cholesterol containing liposomes to attenuate a hypermetabolic response. None of the references of record, alone or in combination, teach a method for using cationic liposomes for treating such a systemic response.

Specifically, there would be no motivation to combine Coffee with either McDonald or Yang since previously there was no teaching or suggestion in the art that cationic cholesterol containing liposomes would be able to attenuate a hypermetabolic response. Briefly, Coffee concerns gel matrices that may comprise growth factors or DNA and suggests that such matrices may be used as wound coverage materials. With-in the gel matrices of Coffee, DNA may be “encapsulated in or complexed with a lipid for transfecting cells,” (paragraph spanning columns 3-4). Thus, Coffee suggests encapsulation of DNA for the purpose of increased transfection of cells. Coffee does not teach or suggest that liposomes *themselves* may be used to treat a wound

or to attenuate a hypermetabolic response. Hence, a skilled artisan seeking to modify the methods of Coffee to attenuate a hypermetabolic response would not be motivated to use liposomes of McDonald or Yang since these references do not concern thermal wounds nor do they concern methods for treating a hypermetabolic response. Thus, there is no explicit or implicit motivation to combine the references of record.

The foregoing arguments notwithstanding, there would be no reasonable expectation of success in the combination of any of the references of record. Specifically, since there was no suggestion in the art regarding the ability of liposomes to attenuate a hypermetabolic response, it would be completely unpredictable that the liposomes of McDonald or Yang could be used for such a purpose. There must be at least some degree of predictability for there to be a reasonable expectation of success (MPEP §2143.03, *In re Rinehart*, 531 F.2d 1048, 189 USPQ 143 (CCPA 1976)). In this case, as evidenced by the declaration of Dr. Jeschke, it was not predictable that cationic/cholesterol liposomes would be able to attenuate a hypermetabolic response. Thus, there would be no expectation of success in the combination of Coffee with either McDonald or Yang. Hence, no *prima facie* case for obviousness has been set forth on the record.

Furthermore, even if a *prima facie* case were set forth, none of the references of record teach or suggest the surprising and unexpected results obtained with the methods of the instant invention. "A greater than expected result is an evidentiary factor pertinent to the legal conclusion of obviousness" *In re Corkill*, 711 F.2d 1496, 226 USPQ 1005 (Fed. Cir. 1985). Such a greater than expected result *is* realized using the methods of the invention. Specifically, the instant methods have a greater than expected effect on wound healing in that they attenuate the systemic hypermetabolic response. As described in the declaration of Dr. Jeschke (submitted herewith) studies set forth in the instant application demonstrate an unexpected systemic effect achieved

when cationic cholesterol containing liposomes are administered locally to a wound site. These effects comprise short term weight gain, increases in serum protein and transferrin levels, and a decrease in serum levels of type I acute phase proteins and proinflammatory cytokines in treated animals. As described by Dr. Jeschke these effects constitute an attenuation of the systemic hypermetabolic response to injury. None, of the prior art of record teaches that locally administered cholesterol containing cationic liposomes could achieve these systemic results. Thus, the systemic effects of the instant methods on hypermetabolic response to injury constitutes a difference *in kind* that would not be predictable from the art of record. Hence, even were a *prima facie* case for obviousness set forth, it would not render obvious the instant claims in view the surprising and unexpected results achieved by the methods of the invention..

Rejection of Claims 5-9, 25-42 as obvious in light of Coffee in view of Yang further in view of Baur, Boyce or Kushner and further in view of Burgess.

Applicants have addressed the rejection of the instant claims over Coffee in view of Yang. None of the other references cited in this rejection are considered relevant to the foregoing arguments thus it is believed that these arguments also render this rejection moot.

Rejection of Claims 5-6 and 9 as obvious over Goldstein in view of McDonald or Yang.

This rejection considered moot in view of the amendments presented herein.

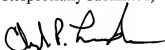
Rejection of Claims 5-6, 9, 25-30 and 39-42 as obvious over Goldstein in view of McDonald or Yang further in view of Coleman

This rejection is also considered moot in view of the amendments presented herein.

C. Conclusions

In view of the foregoing amendments and arguments, Applicants assert that the instant application is in condition for allowance and such favorable action is requested. Should the Examiner have any questions regarding these amendments he is invited to contact the undersigned attorney at (512) 536-3167.

Respectfully submitted,



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Date: November 22, 2006